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| 09/646,399      | 11/01/2000  | Carole Ciolina       | ST98008A            | 8666             |

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EXAMINER

SULLIVAN, DANIEL M

| ART UNIT | PAPER NUMBER |
|----------|--------------|
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1636

DATE MAILED: 11/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

09/646,399

**Applicant(s)**

CIOLINA ET AL.

**Examiner**

Daniel M Sullivan

**Art Unit**

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 31 August 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-42 is/are pending in the application.
- 4a) Of the above claim(s) 10-13 and 39-42 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-3 is/are rejected.
- 7) ☒ Claim(s) 4-9 and 14-38 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 15 September 2000 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 3/14/02.
- ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: \_\_\_\_\_.

### **DETAILED ACTION**

This is the First Office Action on the merits of the application file 1 November 2000 as the US National Stage of international application PCT/FR99/00643, filed 19 March 1999, which claims benefit of US Provisional application 60/058,848, filed 18 May 1998, and French patent application FR 98/03573, filed 24 March 0998. The Preliminary Amendments filed 19 August 2002 and 12 May 2003 have been entered. Claims 1-42 were originally filed. Claim 23 was amended in the 12 May Paper. Claims 1-42 are pending.

### ***Election/Restrictions***

Applicant's election with traverse of Group I (claims 1-9 and 14-37), the intracellular targeting molecule of claim 23, the cationic lipid of claim 29 and the neutral lipid of claim 31 in the reply filed on 31 August 2004 is acknowledged. The traversal is on several grounds.

First, Applicant notes that the European Patent Office, which conducted the International search, found no fault with unity of invention. In that regard, Applicant is reminded that 37 CFR §1.499 provides that the examiner may require the applicant to elect the invention to which the claims shall be restricted "at any time before the final action *at the discretion of the examiner.*" The National stage Examiner is in no way bound by the International proceedings, and, given that restriction is discretionary, the absence of a finding of "lack of unity" in an International application is not evidence that unity of invention exists.

Next, Applicant argues that the Felgner *et al.* reference cited in the restriction requirement does not anticipate the technical feature that unites the claims. Applicant urges, "Felgner *et al.* describes PNA clamps which have two identical PNA sequences joined by a

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flexible hairpin linker containing three 8-amino-3,6-dioxaoctanoic acid units; when a PNA clamp is mixed with a complementary homopurine homopyrimidine DNA target sequence, a PNA-DNA-PNA triplex hybrid can form. Felgner *et al.* does not describe a double-stranded DNA molecule and at least one oligonucleotide coupled to a targeting signal and capable of forming a triple helix with a specific sequence present in the double stranded DNA molecule. The PNA described by Felgner *et al.* form a PNA-DNA-PNA triplex because of the hairpin formed by the PNA. The triplex includes only a single strand of the DNA” (page 3).

This argument has been fully considered but is not deemed persuasive. Applicant appears to be comparing one preferred embodiment of the Felgner *et al.* invention with an embodiment disclosed in the present application to which the instant claims are not limited. The claimed vector is limited to comprising a double stranded DNA molecule and at least one oligonucleotide coupled to a targeting signal and which is capable of forming a triple helix with a specific sequence present on the said double-stranded DNA molecule. Even if the Felgner *et al.* reference only contemplated a PNA clamp, this embodiment would anticipate the presently claimed vector. According to the broadest reasonable interpretation of the claims, the vector need only comprise a double stranded DNA molecule and a specific sequence to which the oligonucleotide binds. There is no requirement that a specific sequence within the double stranded DNA to which the oligonucleotide binds contribute two of the three strands of the triple helix while and the oligonucleotide coupled to a targeting signal provide only one strand. Applicant acknowledges that the oligonucleotide of Felgner *et al.* is “capable of forming a triple helix”, albeit a PNA-DNA-PNA triple helix, and Felgner *et al.* clearly teaches that the vector contemplated therein

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can comprise double stranded DNA (see, *e.g.*, column 3, lines 30-32). Thus, Felgner *et al.* teaches a vector comprising all of the limitations of the vector claimed in the instant application.

Furthermore, even if the claimed invention were limited such that the oligonucleotide provides only a single strand of the triple helix, the technical feature would not represent an inventive step over the teachings of Felgner *et al.* By several teachings, Felgner *et al.* suggests that triplex forming oligonucleotides other than the PNA clamp exemplified in the drawings can be used to attach the targeting signal to the vector. In column 6, lines 48-54, Felgner *et al.* teaches that a PNA or PNA clamp can be used as the PNA probe. Further, in the first full paragraph in column 11, Felgner *et al.* teaches, "other molecules which are capable of triplex formation and hybridization in a sequence-specific manner to DNA are also contemplated such as those described in U.S. Pat. No. 5,460,941" and the cited '941 patent teaches formation of triplex DNA between a duplex DNA and a homologous oligonucleotide (see especially Figure 1 and the caption thereto). Therefore, the embodiment of the invention that Applicant describes in the traverse would at least be obvious over the teachings of Felgner *et al.*

Finally, Applicant submits that restriction to examination of a single species of targeting signal, transfecting agent and adjuvant is improper because, "[w]herein related species are recited in the same claim, there is unity of invention as long as the species are of the same nature" (bridging pages 3-4). This argument is found persuasive with respect to the transfecting agents and adjuvants; therefore the restriction requirement among the transfecting agents and adjuvants of claims 28-33 is withdrawn and all of the species will be examined together.

However, Applicant's argument for rejoinder of the targeting signals of claims 21-25 is not deemed persuasive. It is believed that the statement cited in the traverse is actually found in

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MPEP 1850 §(B), which pertains to unity of invention for Markush type claims. The section goes on to state:

When the Markush grouping is for alternatives of chemical compounds, they shall be regarded as being of a similar nature where the following criteria are fulfilled:

(A) All alternatives have a common property or activity; and

(B)(1) A common structure is present, i.e., a significant structural element is shared by all of the alternatives; or

(B)(2) In cases where the common structure cannot be the unifying criteria, all alternatives belong to a recognized class of chemical compounds in the art to which the invention pertains.

In the instant case, vectors comprising the targeting signals set forth in the claims share the broad functional property of being targeted; however, no special technical feature exists among the vectors comprising the targeting signals because the structures which impart the common property do not share a significant structural element and, as stated in the restriction requirement, Felgner *et al.* anticipates the general technical feature of a targeting signal, which is the unifying functional property. See also, Examples 35 in Chapter 10 of the International Search and Preliminary Examination Guidelines, which can be obtained from WIPO's web site ([www.wipo.int/pct/en/texts/gdlines.htm](http://www.wipo.int/pct/en/texts/gdlines.htm)).

The requirement is still deemed proper and is therefore made FINAL.

In accordance with "Unity of Invention" practice, the first method of using the elected product, (*i.e.*, Group VII, claim 38, directed to a method for the manufacture of a medicament), will be examined with the product. Therefore, claim 38 is rejoined.

Claims 10-13 and 39-42 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

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Claims 1-9 and 14-38, and the intracellular targeting molecule of claim 23 are presently under consideration.

### ***Priority***

If applicant desires priority under 35 U.S.C. 119(e) based upon a previously filed application, specific reference to the earlier filed application must be made in the instant application. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph unless it appears in an application data sheet. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No. \_\_\_\_" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

If the application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months

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from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A priority claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed claim for priority under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

Please note that the Provisional application 60/085,848 is filed in a language other than English. Applications that claim benefit of a provisional application filed in a non-English language must include an English translation of the non-English language provisional application and a statement that the translation is accurate. See 37 CFR 1.78(a)(5). The English translation and a statement that the translation is accurate as required by 37 CFR 1.78(a)(5) is missing. If Applicant wishes to claim benefit of the Provisional application, the missing English translation and a statement that the translation is accurate should be supplied in the reply to this Office action prior to the expiration of the time period set in this Office action.



### ***Claim Objections***

Claims 4-9 and 14-38 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only and cannot depend from any other multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claims 4-9 and 14-38 have not been further treated on the merits.

Claims 1-3 are objected to because of the following informalities: The claims are not written as complete sequences. Specifically, proper English grammar dictates that the claims should begin with a definite or indefinite article. It is recommended that claim 1, and all other independent claims be amended to begin with "A", and claims 2 and 3 be amended to begin with "The".

Appropriate correction is required.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-3 are rejected under 35 U.S.C. 102(e) as being anticipated by Felgner *et al.* U.S.

Patent No. 6,165,720 (effective filing date 18 September 1997; previously made of record).

As discussed herein above, the claimed vector is limited to comprising a double stranded DNA molecule and at least one oligonucleotide coupled to a targeting signal and which is capable of forming a triple helix with a specific sequence present on the said double-stranded DNA molecule.

Felgner *et al.* teaches a nucleic acid molecule and a conjugated peptide nucleic acid (PNA) molecule (which is encompassed within the scope of the present oligonucleotide as evidenced by the paragraph bridging 17-19 of the specification) associated with said DNA molecule, wherein the PNA molecule contains a region complementary to the DNA molecule. Felgner *et al.* further teaches that the PNA is preferably conjugated to a peptide that is a nuclear localization signal peptide and that the DNA molecule is preferably a circular double stranded DNA (see throughout, especially the second full paragraph in column 3). In Figure 3 and the caption thereto and in the first full paragraph in column 11, Felgner *et al.* teaches that the oligonucleotide is structured such that it is associated with the DNA molecule via a triple helix with a specific sequence present in the DNA molecule. Thus, Felgner *et al.* teaches a vector for transferring nucleic acids comprising all of the limitations of the instant claim 1.

The vector of Felgner *et al.* is a plasmid according to claim 2 (*Id.*), which can be circular (see especially column 3, line 31) or supercoiled (see especially column 15, lines 40-42 and Example 5) according to claim 3.

Felgner *et al.* teaches a vector comprising each of the limitations of the instant claimed invention; therefore, the claims are anticipated by Felgner *et al.*

### ***Conclusion***

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 571-272-0779. The examiner can normally be reached on Monday through Thursday 6:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

A handwritten signature in black ink, appearing to read 'D Sullivan', with a long horizontal flourish extending to the right.

Daniel M Sullivan, Ph.D.  
Examiner  
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